

Amendment and Response Under 37 C.F.R. §1.116 - Expedited Examining Procedure

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Serial No.: 09/829,872

Confirmation No.: 7416

Filed: April 10, 2001

For: NUCLEAR MAGNETIC RESONANCE METHODS FOR IDENTIFYING SITES IN PAPILLOMAVIRUS E2 PROTEIN

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. **(Currently Amended)** A nuclear magnetic resonance method for identifying a site in a DNA-binding and dimerization domain of an HPV-18 strain of papillomavirus E2 protein, the method comprising:

providing a first set of chemical shifts for atoms of a mixture comprising a ligand and the HPV-18 strain of papillomavirus E2 protein; wherin the chemical shifts are assigned to atoms of the protein;

comparing the first set of chemical shifts to a second set of chemical shifts as listed in Table 1; and

identifying at least a portion of the atoms that exhibit changes in chemical shifts, wherein the site comprises the identified atoms and is a ligand binding site.

2. **(Previously Presented)** The method of claim 1 wherein providing the first set of chemical shifts comprises:

providing a mixture of the ligand and the HPV-18 strain of papillomavirus E2 protein;
allowing the ligand to interact with the HPV-18 strain of papillomavirus E2 protein;
obtaining a nuclear magnetic resonance spectrum of the mixture; and
measuring chemical shifts of atoms from the spectrum.

3. **(Original)** The method of claim 2 wherein allowing the ligand to interact comprises allowing the ligand and the protein to reach a binding equilibrium.

4-5. **(Canceled)**

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6. **(Previously Presented)** The method of claim 1 wherein identifying at least a portion of the atoms comprises identifying at least one proton that either exhibits a change in ¹H chemical shift of at least about 0.04 ppm or is no longer observed.

7. **(Original)** The method of claim 1 wherein identifying at least a portion of the atoms comprises identifying at least one carbon atom that either exhibits a change in ¹³C chemical shift of at least about 0.2 ppm or is no longer observed.

8. **(Original)** The method of claim 1 wherein identifying at least a portion of the atoms comprises identifying at least one nitrogen atom that either exhibits a change in ¹⁵N chemical shift of at least about 0.2 ppm or is no longer observed.

9. **(Withdrawn-Currently Amended)** A nuclear magnetic resonance method for identifying a site in a DNA-binding and dimerization domain of an HPV-18 strain of papillomavirus E2 protein, the method comprising:

providing a first ¹H-¹⁵N heteronuclear single quantum correlation spectrum of a mixture comprising a ligand and the HPV-18 strain of papillomavirus E2 protein;

comparing the first ¹H-¹⁵N heteronuclear single quantum correlation spectrum to a second ¹H-¹⁵N heteronuclear single quantum correlation spectrum as illustrated in Figure 2; and

identifying at least a portion of the amino acids having atoms that exhibit changes in chemical shifts, wherein the site comprises the identified amino acids and is a ligand binding site.

10. **(Withdrawn)** The method of claim 9 wherein providing the first spectrum comprises: providing a mixture of the ligand and the HPV-18 strain of papillomavirus E2 protein; allowing the ligand to interact with the HPV-18 strain of papillomavirus E2 protein; and obtaining a ¹H-¹⁵N heteronuclear single quantum correlation spectrum of the mixture.

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11. (Withdrawn) The method of claim 10 wherein allowing the ligand to interact comprises allowing the ligand and the protein to reach a binding equilibrium.

12-13. (Canceled)

14. (Withdrawn) The method of claim 9 wherein identifying at least a portion of the amino acids comprises identifying at least one amino acid having a proton that either exhibits a change in ¹H chemical shift of at least about 0.04 ppm or is no longer observed.

15. (Withdrawn) The method of claim 9 wherein identifying at least a portion of the amino acids comprises identifying at least one amino acid having a nitrogen atom that either exhibits a change in ¹⁵N chemical shift of at least about 0.2 ppm or is no longer observed.

16. (Canceled)

17. (Previously Presented) A computer-assisted method for identifying a ligand binding site in a DNA-binding and dimerization domain of an HPV-18 strain of papillomavirus E2 protein, the method comprising:

providing a first set of nuclear magnetic resonance chemical shifts for atoms of a mixture comprising the ligand and the HPV-18 strain of papillomavirus E2 protein; wherein the chemical shifts are assigned to atoms of the protein;

causing the first set of chemical shifts to be entered into memory of a computer;

causing the computer to read a second set of chemical shifts as listed in Table 1 from a machine-readable data storage medium;

causing the computer to compare the first and second sets of chemical shifts; and

causing the computer to identify at least a portion of the atoms that exhibit changes in chemical shifts, wherein the ligand binding site comprises the identified atoms.

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18. (Canceled)

19. (Original) The method of claim 17 wherein causing the computer to identify at least a portion of the atoms comprises causing the computer to identify at least one proton that either exhibits a change in ¹H chemical shift of at least about 0.04 ppm or is no longer observed.

20. (Original) The method of claim 17 wherein causing the computer to identify at least a portion of the atoms comprises causing the computer to identify at least one carbon atom that either exhibits a change in ¹³C chemical shift of at least about 0.2 ppm or is no longer observed.

21. (Original) The method of claim 17 wherein causing the computer to identify at least a portion of the atoms comprises causing the computer to identify a nitrogen atom that either exhibits a change in ¹⁵N chemical shift of at least about 0.2 ppm or is no longer observed.

22. (Original) The method of claim 17 further comprising causing the computer to visually display a spatial arrangement of atoms of the ligand binding site.